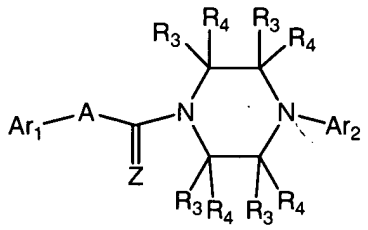
In the claims:

Cancel claims 1-3, 7, 24, 86, 87, 177-192, and 194-196.

Please enter amended claims 4, 5, 8, 9, 26, 27, 31, 32, 37, 40, 42, 44, 46, 48, 59, 62, 63, 161, and 169 as follows:

4. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, $NR_ACR_BR_B'$, $CR_B\ R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and alkyl;

Z is oxygen or sulfur;

each R_3 and R_4 is independently

(a) selected from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO; optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl;

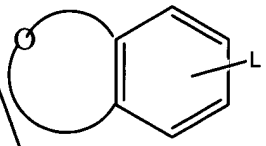
optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted -$S(O)_nNH$alkyl; optionally substituted -$S(O)_nN$(alkyl)(alkyl); optionally substituted -NHC(=O)alkyl; optionally substituted -NC(=O)(alkyl)(alkyl); optionally substituted -$NHS(O)_n$alkyl; optionally substituted -$NS(O)_n$(alkyl)(alkyl); optionally substituted saturated or partially unsaturated heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

(b) joined to a R_3 or R_4 not attached to the same carbon to form an optionally substituted aryl ring, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms selected from N, O, and S;

Ar_1 is selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5; and

(b) bicyclic oxygen-containing groups of the formula:



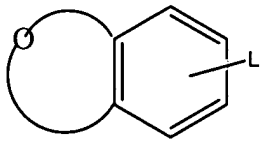
optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

Ar_2 is selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl,

triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5; and

(b) bicyclic oxygen-containing groups of the formula:



optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R_5 is independently selected at each occurrence from the group consisting of halogen, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, -S(O)$_n$(C_{1-4}alkyl), halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, CO(C_{1-

$_4$alkyl), CONH(C_{1-4}alkyl), CON(C_{1-4}alkyl$_1$)(C_{1-4}alkyl$_2$) where alkyl$_1$ and alkyl$_2$ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, $-O-$, $-S(O)_n-$, $-NH-$, $-NR_8-$, $-C(=O)-$, $-C(=O)O-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), $-NHS(O)_n$(alkyl), $-S(O)_n$(alkyl), $-S(O)_nNH$(alkyl), $-S(O)_nN$(alkyl$_3$)(alkyl$_4$) where alkyl$_3$ and alkyl$_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and

containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

5. (Amended) A compound or salt according to Claim 4, wherein:

R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and C_{1-6}alkyl;

each R_3 and R_4 is independently

(a) chosen from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6; C_{2-6}alkynyl substituted with 0-2 R_6; C_{1-6}alkoxy substituted with 0-2 R_6, -NH(C_{1-6}alkyl) substituted

with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y; or

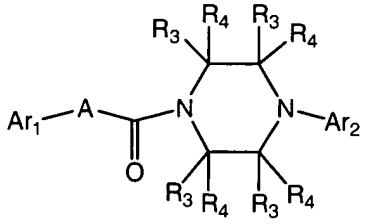
(b) joined to a R_3 or R_4 not attached to the same carbon to form an aryl ring substituted with 0-3 R_6, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(C_{1-4}alkyl), -N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl), -NHS(O)$_n$(C_{1-4}alkyl), -S(O)$_n$(C_{1-4}alkyl), -S(O)$_n$NH(C_{1-4}alkyl), -S(O)$_n$N(C_{1-4}alkyl$_3$)(C_{1-4}alkyl$_4$) where C_{1-4}alkyl$_3$ and C_{1-4}alkyl$_4$ are

optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y'; and

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which are unsubstituted or substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S.

8. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, $CR_B\ R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen or alkyl;

each R_3 and R_4 is independently

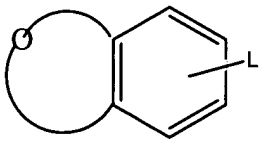
(a) selected from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted $-S(O)_nNHalkyl$; optionally substituted $-S(O)_nN(alkyl)(alkyl)$; optionally substituted $-NHC(=O)alkyl$; optionally substituted $-NC(=O)(alkyl)(alkyl)$; optionally substituted $-NHS(O)_nalkyl$; optionally substituted $-NS(O)_n(alkyl)(alkyl)$; optionally substituted saturated or partially unsaturated heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

(b) joined to a R_3 or R_4 not attached to the same carbon to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

Ar_1 and Ar_2 are independently selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl; wherein Ar_1 is optionally mono-, di-, or trisubstituted with R_5, and Ar_2 is optionally mono-, di-, or trisubstituted with R_9; and

(b) groups of the formula:



optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R_5 is independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R_6, alkenyl substituted with 0-2 R_6, alkynyl substituted with 0-2 R_6, alkoxy and Y;

R_9 is independently selected at each occurrence from the group consisting of nitro, haloalkoxy, hydroxy, amino, alkyl substituted with 0-2 R_6, alkenyl substituted with 0-2 R_6, alkynyl substituted with 0-2 R_6, alkoxy substituted with 0-2 R_6, and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, -$S(O)_n$(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON(alkyl$_1$)(alkyl$_2$) where alkyl$_1$ and alkyl$_2$ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing

1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, -O-, $-S(O)_n-$, -NH-, $-NR_8-$, $-C(=O)-$, $-C(=O)O-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

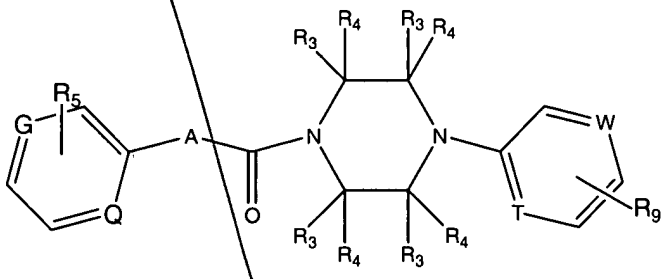
R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), $-NHS(O)_n(alkyl)$, $-S(O)_n(alkyl)$, $-S(O)_nNH(alkyl)$, $-S(O)_nN(alkyl_3)(alkyl_4)$ where $alkyl_3$ and $alkyl_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which are unsubstituted or substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

9. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

G, Q, T, and W are the same or different and are selected from the group consisting of N, CH, and CR_5, wherein T or W or both is N;

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, $CR_B\ R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where

R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and alkyl;

Z is oxygen or sulfur;

each R_3 and R_4 is independently

(a) selected from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO; optionally substituted C_{1-6}alkyl; optionally substituted C_{2-6}alkenyl; optionally substituted C_{2-6}alkynyl; optionally substituted C_{1-6}alkoxy; optionally substituted mono or di(C_{1-6})alkylamino; optionally substituted C_{1-6}alkylthio; optionally substituted C_{1-6}alkyl ketone; optionally substituted C_{1-6}alkylester; optionally substituted C_{1-6}alkylsulfinyl; optionally substituted C_{1-6}alkylsulfonyl; optionally substituted mono- or di(C_{1-6})alkylcarboxamide; optionally substituted -$S(O)_n$NH C_{1-6}alkyl; optionally substituted -$S(O)_n$N(C_{1-6}alkyl)(C_{1-6}alkyl); optionally substituted -NHC(=O) C_{1-6}alkyl; optionally substituted -NC(=O)(C_{1-6}alkyl)(C_{1-6}alkyl); optionally substituted -NHS$(O)_n$$C_{1-6}$alkyl; optionally substituted -NS$(O)_n$(C_{1-6}alkyl)(C_{1-6}alkyl); optionally substituted saturated or partially unsaturated heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3

rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

(b) joined to a R_3 or R_4 not attached to the same carbon to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R_5 represents 1 to 3 substituents independently selected at each occurrence from the group consisting of cyano, hydroxy, amino, C_{3-6} alkyl substituted with 0-2 R_6, C_{2-6} alkenyl substituted with 0-2 R_6, C_{2-6} alkynyl substituted with 0-2 R_6, C_{3-6} alkoxy, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y;

R_9 represents 0 to 3 substituents independently selected at each occurrence from the group consisting of halogen, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl

substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy substituted with 0-2 R_6, and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, $-S(O)_n(C_{1-4}alkyl)$, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, $CO(C_{1-4}alkyl)$, $CONH(C_{1-4}alkyl)$, $CON(C_{1-4}alkyl_1)(C_{1-4}alkyl_2)$ where $alkyl_1$ and $alkyl_2$ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, -O-, $-S(O)_n-$, -NH-, $-NR_8-$, -C(=O)-, -C(=O)O-, -C(=O)NH-, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, NHC(=O)-, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

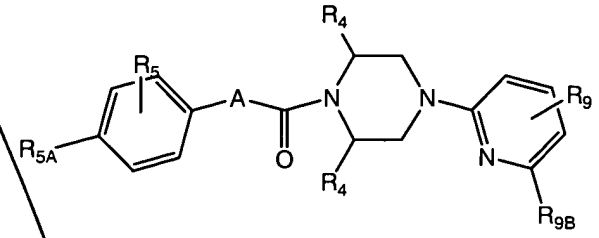
R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo,

hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, $-NHC(O)(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl)$, $-NHS(O)_n(C_{1-4}alkyl)$, $-S(O)_n(C_{1-4}alkyl)$, $-S(O)_nNH(C_{1-4}alkyl)$, $-S(O)_nN(C_{1-4}alkyl_3)(C_{1-4}alkyl_4)$ where $C_{1-4}alkyl_3$ and $C_{1-4}alkyl_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which are unsubstituted or substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, $C_{1-4}alkyl$, $C_{1-4}alkoxy$, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and $C_{1-4}alkylthio$; wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

26. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of NH, -CH=CH-, and CH_2NH;

R_4 is independently chosen from hydrogen and C_{1-4} alkyl;

R_5 represents 0 to 2 substituents independently chosen at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, and -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6;

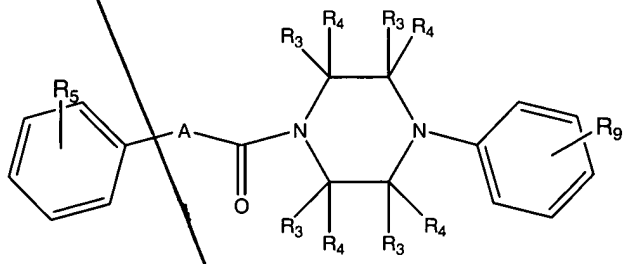
R_9 represents 0 to 2 substituents and is independently chosen at each occurrence from the group consisting of halogen, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, and C_{1-6}alkoxy substituted with 0-2 R_6.

R_{5A} is independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-6} alkoxy, -NH(C_{1-6} alkyl), and -N(C_{1-6} alkyl)(C_{1-6} alkyl);

R_{9B} is independently selected from the group consisting of halogen, nitro, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6} alkyl, and C_{1-6} alkoxy; and

R_6 is independently selected at each occurrence the group consisting of halogen, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, -NH(C_{1-4} alkyl), and -N(C_{1-4} alkyl)(C_{1-4} alkyl).

27. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of a single bond, S, NR_A, NR_ACHR_B, CHR_BNR_A, -CR_A=CR_B-, and C_3H_4; where R_A and R_B are independently selected at each occurrence from the group consisting of hydrogen and alkyl;

each R_3 and R_4 is independently

(a) selected from the group consisting of hydrogen; halogen; hydroxy; amino; cyano; nitro; -COOH; -CHO, optionally substituted alkyl; optionally substituted alkenyl; optionally substituted alkynyl; optionally substituted alkoxy; optionally substituted mono or dialkylamino; optionally substituted alkylthio; optionally substituted alkyl ketone; optionally substituted alkylester; optionally substituted alkylsulfinyl; optionally substituted alkylsulfonyl; optionally substituted mono- or di-alkylcarboxamide; optionally substituted -$S(O)_nNH$alkyl; optionally substituted -$S(O)_nN$(alkyl)(alkyl); optionally substituted -NHC(=O)alkyl; optionally substituted -NC(=O)(alkyl)(alkyl); optionally substituted -$NHS(O)_n$alkyl; optionally substituted -$NS(O)_n$(alkyl)(alkyl); optionally substituted saturated or partially unsaturated heterocycle of from 5 to 8 atoms, which saturated or partially unsaturated heterocycle contains 1, 2, or 3 heteroatoms independently selected from N, O, and S; optionally substituted aryl having from 1 to 3 rings; and optionally substituted heteroaryl, said heteroaryl having from 1 to 3 rings, 5 to 8 ring members in each ring and, in at least one of said rings, from 1 to about 3 heteroatoms per ring independently selected from the group consisting of N, O, and S; or

(b) joined to a R_3 or R_4 not attached to the same carbon to form an optionally substituted aryl ring; a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is optionally substituted; or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is optionally substituted and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R_5 represents 0-3 substituents independently selected at each occurrence from the group consisting of cyano, nitro, haloalkyl, haloalkoxy, C_{2-6} alkenyl substituted with 0-2 R_6, and C_{2-6} alkynyl substituted with 0-2 R_6;

R_9 represents 0-3 substituents independently selected at each occurrence from the group consisting of bromo, haloalkyl, haloalkoxy, hydroxy, C_{2-6} alkyl substituted with 0-2 R_6, C_{2-6} alkenyl substituted with 0-2 R_6, C_{2-6} alkynyl substituted with 0-2 R_6, and C_{2-6} alkoxy;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, alkyl, alkoxy, -$S(O)_n$(alkyl), haloalkyl, haloalkoxy, CO(alkyl), CONH(alkyl), CON($alkyl_1$)($alkyl_2$) where $alkyl_1$ and $alkyl_2$ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing

1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, -O-, $-S(O)_n-$, -NH-, $-NR_8-$, $-C(=O)-$, $-C(=O)O-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, NHC(=O)-, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 3 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 3 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(alkyl), -NH(alkyl), -N(alkyl)(alkyl), -NHC(O)(alkyl), -N(alkyl)C(O)(alkyl), $-NHS(O)_n$(alkyl), $-S(O)_n$(alkyl), $-S(O)_nNH$(alkyl), $-S(O)_nN(alkyl_3)(alkyl_4)$ where $alkyl_3$ and $alkyl_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

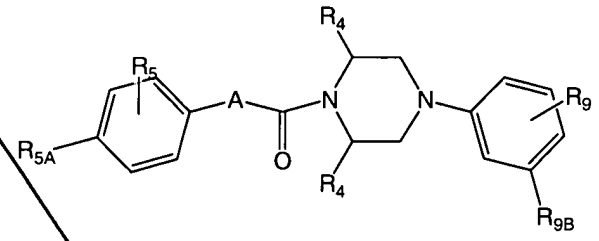
Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are

saturated, unsaturated, or aromatic, which are unsubstituted or substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, alkyl, alkoxy, haloalkyl, haloalkoxy, mono- or dialkylamino, and alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

30. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is selected from the group consisting of NH, -CH=CH-, and CH_2NH;

R_4 is independently selected at each occurrence from hydrogen and C_{1-4}alkyl;

R_5 represents 0 to 2 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, amino, C_{2-6}alkenyl

substituted with 0-2 R_6, and C_{2-6}alkynyl substituted with 0-2 R_6;

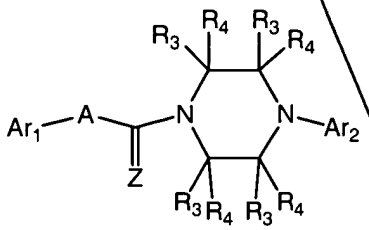
R_9 represents 0 to 2 substituents and is independently selected at each occurrence from the group consisting of halogen, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, and C_{1-6}alkoxy substituted with 0-2 R_6;

R_{5A} is independently selected from the group consisting of halogen, cyano, nitro, trifluoromethyl, trifluoromethoxy, hydroxy, amino, C_{1-6} alkyl, C_{1-6} alkoxy, -NH(C_{1-6} alkyl), and -N(C_{1-6} alkyl)(C_1-C_6 alkyl);

R_{9B} is independently selected from the group consisting of trifluoromethoxy, hydroxy, C_{2-6} alkyl, and C_{2-6} alkoxy; and

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, C_{1-4} alkyl, and C_{1-4} alkoxy.

31. (Amended) A compound of the formula:



or a pharmaceutically acceptable salt thereof, wherein the compound or pharmaceutically acceptable salt thereof

exhibits an EC50 or K_i of 1 micromolar or less in a standard assay of capsaicin receptor mediated calcium mobilization; and wherein

A is absent or is selected from the group consisting of O, S, NR_A, $NR_ACR_BR_B'$, $CR_B\ R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and C_{1-6} alkyl;

Z is oxygen or sulfur;

each R_3 and R_4 is independently

(a) selected from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6; C_{2-6}alkynyl substituted with 0-2 R_6; C_{1-6}alkoxy substituted with 0-2 R_6, $-NH(C_{1-6}alkyl)$ substituted with 0-2 R_6, $-N(C_{1-6}alkyl)(C_{1-6}alkyl)$ where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y; or

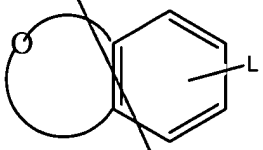
(b) joined to a R_3 or R_4 not attached to the same carbon to form an aryl ring substituted with 0-3 R_6, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1,

2, or 3 heteroatoms independently selected from N, O, and S;

Ar_1 is selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, phenyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5; and

(b) bicyclic oxygen-containing groups of the formula:

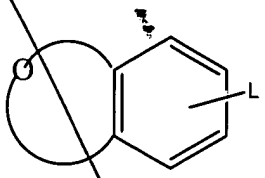


optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

Ar_2 is selected from the group consisting of:

(a) cyclohexyl, cyclopentyl, piperidinyl, piperazinyl, pyrrolyl, furanyl, thienyl, pyrazolyl, imidazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, triazolyl, tetrazolyl, pyridyl, pyrimidyl, pyrazinyl, benzimidazolyl, naphthyl, indolyl, isoindolyl, benzofuranyl, isobenzofuranyl, benzo[b]thiophenyl, benz[d]isoxazolyl, quinolinyl, isoquinolinyl, cinnolinyl, quinazolinyl, and quinoxalinyl, each of which is optionally mono-, di-, or trisubstituted with R_5; and

(b) bicyclic oxygen-containing groups of the formula:



optionally mono-, di-, or trisubstituted with R_5, where L represents point of attachment and may be at any point on the benzene ring, and the oxygen-containing ring of the bicyclic oxygen-containing group consists of from 5 to 8 ring atoms, contains 1 or 2 oxygen atoms and remaining ring atoms are carbon;

R_5 is independently selected at each occurrence from the group consisting of halogen, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy, and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, $-S(O)_n(C_{1-4}alkyl)$, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, $CO(C_{1-4}alkyl)$, $CONH(C_{1-4}alkyl)$, $CON(C_{1-4}alkyl_1)(C_{1-4}alkyl_2)$ where $alkyl_1$ and $alkyl_2$ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, $-O-$, $-S(O)_n-$, $-NH-$, $-NR_8-$, $-C(=O)-$, $-C(=O)O-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-4}alkyl)$, $-NHC(O)(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl)$, $-NHS(O)_n(C_{1-4}alkyl)$, $-S(O)_n(C_{1-}$

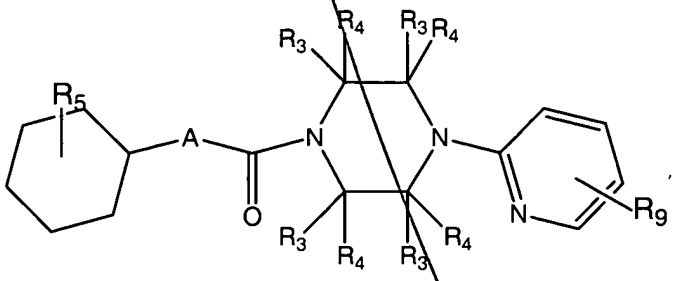
$_4$alkyl), -S(O)$_n$NH(C_{1-4}alkyl), -S(O)$_n$N(C_{1-4}alkyl$_3$)(C_{1-4}alkyl$_4$) where C_{1-4}alkyl$_3$ and C_{1-4}alkyl$_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio;

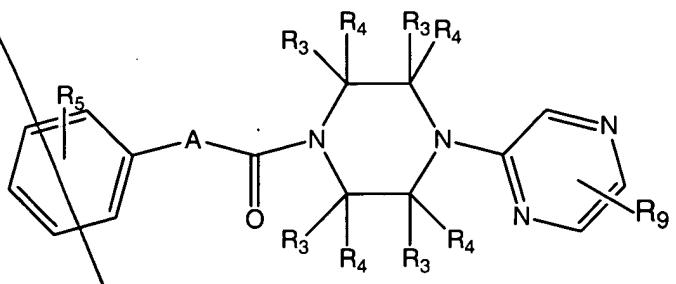
wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

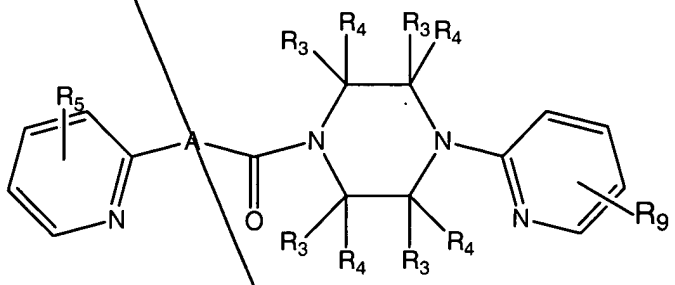
32. (Amended) A compound of the Formula A, Formula B, Formula C, Formula D, Formula E, or Formula F:



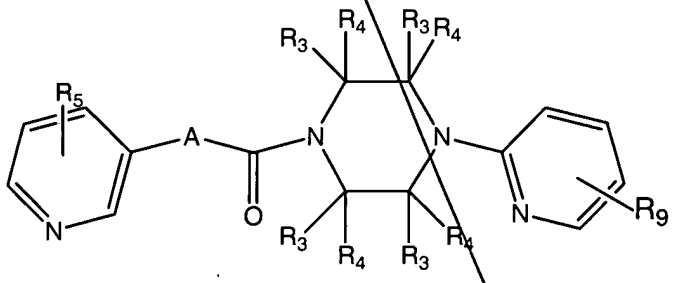
Formula A



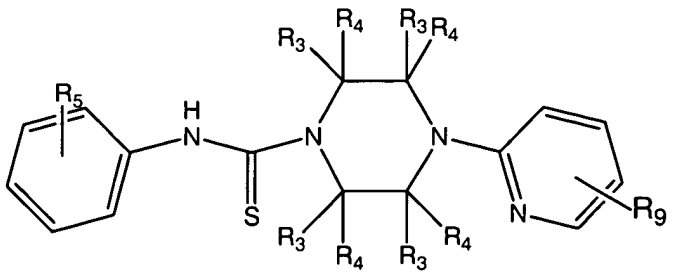
Formula B



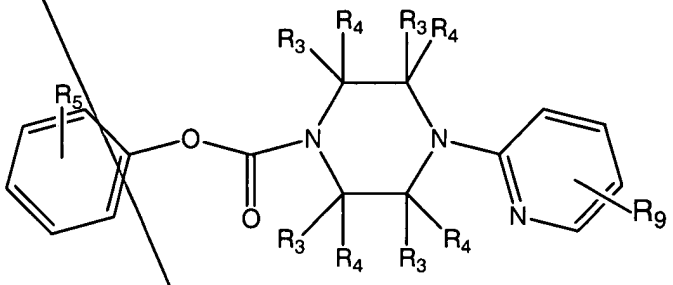
Formula C



Formula D



Formula E



Formula F

or a pharmaceutically acceptable salt of Formula A, Formula B, Formula C, Formula D, Formula E, or Formula F, wherein

A represents NH or O;

each R_3 and R_4 is independently

(a) selected from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6; C_{2-6}alkynyl substituted with 0-2 R_6; C_{1-6}alkoxy substituted with 0-2 R_6, -NH(C_{1-6}alkyl) substituted

with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, -XR_7, and Y; or

(b) joined to a R_3 or R_4 not attached to the same carbon to form an aryl ring substituted with 0-3 R_6, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R_5 represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, -XR_7, and Y;

R_9 represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl

substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy substituted with 0-2 R_6, and Y;

R_6 is independently selected at each occurrence from the group consisting of halogen, hydroxy, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, $-S(O)_n(C_{1-4}alkyl)$, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, $CO(C_{1-4}alkyl)$, $CONH(C_{1-4}alkyl)$, $CON(C_{1-4}alkyl_1)(C_{1-4}alkyl_2)$ where $alkyl_1$ and $alkyl_2$ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

B/ Sub C1

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, $-O-$, $-S(O)_n-$, $-NH-$, $-NR_8-$, $-C(=O)-$, $-C(=O)O-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms is unsubstituted or substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, $-O(C_{1-4}alkyl)$, $-NH(C_{1-4}alkyl)$, $-N(C_{1-4}alkyl)(C_{1-}$

B

$_4$alkyl), -NHC(O)(C_{1-4}alkyl), -N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl), -NHS(O)$_n$(C_{1-4}alkyl), -S(O)$_n$(C_{1-4}alkyl), -S(O)$_n$NH(C_{1-4}alkyl), -S(O)$_n$N(C_{1-4}alkyl$_3$)(C_{1-4}alkyl$_4$) where C_{1-4}alkyl$_3$ and C_{1-4}alkyl$_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

37. (Amended) A compound or salt according to Claim 32, wherein:

A represents NH;

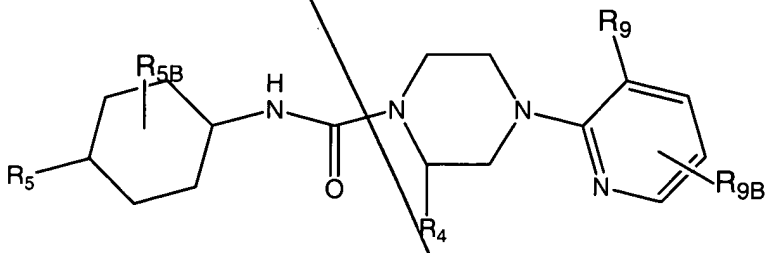
R_3 represents hydrogen;

R_4 is independently chosen at each occurrence from hydrogen and methyl; and

R_5 represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_9 represents from 1 to 3 substituents independently selected at each occurrence from the group consisting of halogen, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, and C_{3-8} cycloalkyl.

38. (Amended) A compound or salt of the Formula A-1



Formula A-1

wherein

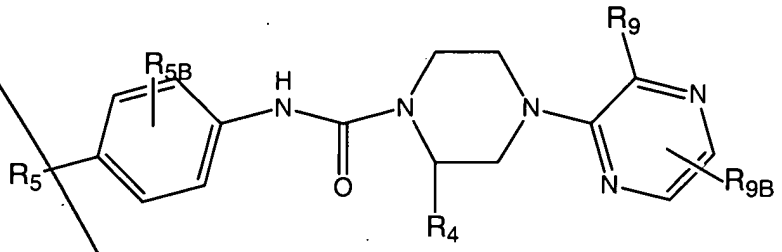
R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-}

$_6$alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

40. (Amended) A compound or salt of Formula B-1



Formula B-1

wherein

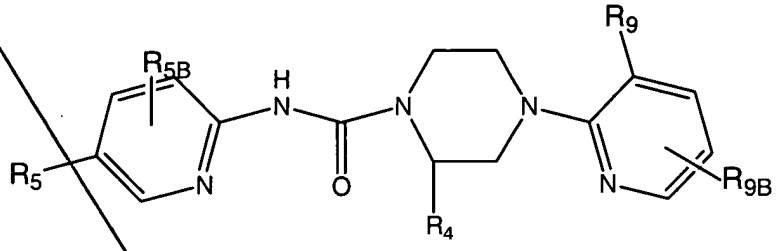
R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-}

$_3$alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

42. (Amended) A compound or salt of Formula C-1



Formula C-1

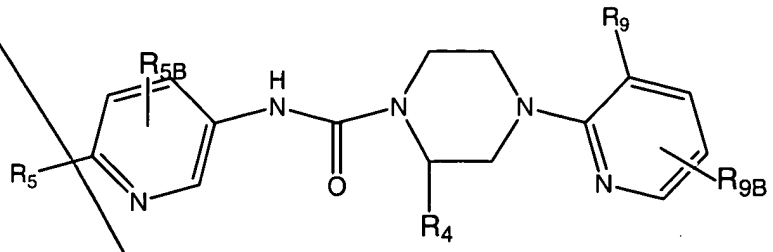
wherein:

R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

44. (Amended) A compound or salt [according to Claim 37] of Formula D-1



Formula D-1

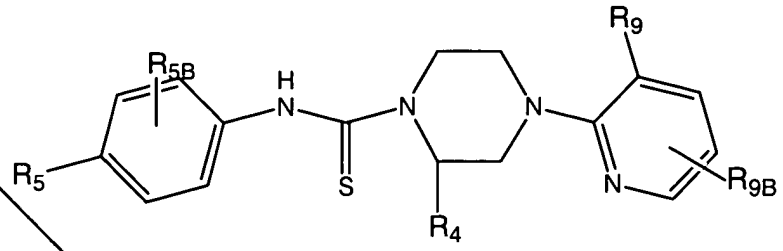
wherein:

R_5 is selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl;

R_9 is selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

46. (Amended) A compound or salt of Formula E-1



Formula E-1

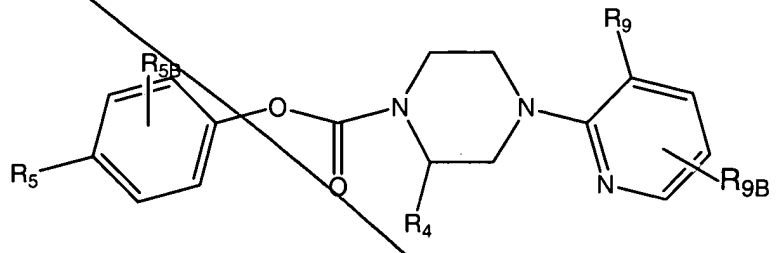
wherein:

R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

48. (Amended) A compound of salt of Formula F-1



Formula F-1

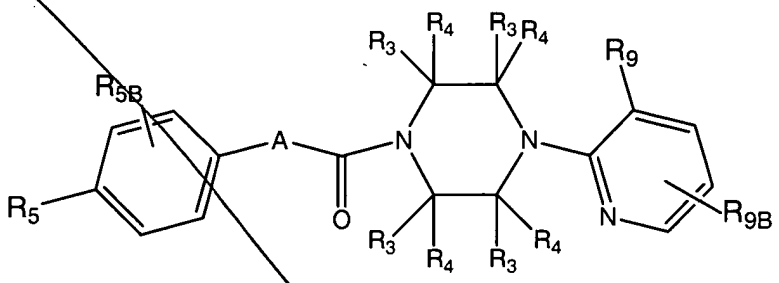
wherein:

R_4 is hydrogen or methyl;

R_5 and R_9 are independently selected from the group consisting of halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), -N(C_{1-6}alkyl)(C_{1-6}alkyl), and C_{3-8} cycloalkyl; and

R_{5B} and R_{9B} each represent from 0 to 2 substituents independently selected at each occurrence from hydrogen, halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, hydroxy, amino, C_{1-3}alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl).

50. (Amended) A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, CR_B $R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where

R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and C_{1-6} alkyl;

each R_3 and R_4 is independently

(a) selected from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6; C_{2-6}alkynyl substituted with 0-2 R_6; C_{1-6}alkoxy substituted with 0-2 R_6, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, $-XR_7$, and Y; or

(b) joined to a R_3 or R_4 not attached to the same carbon to form an aryl ring substituted with 0-3 R_6, a saturated or partially unsaturated carbocyclic ring of from 5 to 8 members, which carbocyclic ring is substituted with 0-2 R_6, or a saturated, partially unsaturated, or aromatic heterocyclic ring of from 5 to 8 members, which heterocyclic ring is substituted with 0-2 R_6 and contains 1, 2, or 3 heteroatoms independently selected from N, O, and S;

R_5 is selected from the group consisting of bromo, fluoro, iodo, halo(C_{1-6})alkyl, halo(C_{3-6})alkoxy, C_{3-6}alkyl substituted with 0-3 R_6, C_{2-6}alkenyl substituted with 0-3 R_6, C_{2-6}alkynyl substituted with 0-3 R_6, C_{3-6}alkoxy, (C_{3-8}cycloalkyl)C_{1-4}alkyl,

-NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is substituted with 0-2 R_6, Y, -(C=O)Y, -(CH_2)Y, and -(CH(CN))Y;

R_9 is selected from the group consisting of halogen, cyano, -N(SO_2C_{1-6}alkyl)(SO_2C_{1-6}alkyl),-SO_2NH_2, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, C_{1-6}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, and C_{1-6}alkoxy substituted with 0-2 R_6;

R_{5B} represents from 0 to 2 substituents independently selected at each occurrence from the group consisting of

(a) halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, (C_{3-8}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy, -NH(C_{1-6}alkyl) substituted with 0-2 R_6, -N(C_{1-6}alkyl)(C_{1-6}alkyl) where each C_{1-6}alkyl is independently substituted with 0-2 R_6, and Y; and

(b) groups that are joined to R_5 to form a C_{3-8}cycloalkyl group or a saturated or partially unsaturated heterocycle, each of which is optionally substituted by from 1 to 5 substituents independently chosen from cyano, halogen, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), halo(C_{1-4})alkyl, and halo(C_{1-4})alkoxy, wherein the saturated or partially unsaturated heterocyclecontains from

4 to 8 ring atoms of which 1, 2, or 3 are heteroatoms independently selected from N, O, and S;

R_{9B} represents from 0 to 2 substituents independently selected at each occurrence from halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl substituted with 0-2 R_6, (C_{3-8}cycloalkyl)C_{1-4}alkyl substituted with 0-2 R_6, C_{2-6}alkenyl substituted with 0-2 R_6, C_{2-6}alkynyl substituted with 0-2 R_6, C_{1-6}alkoxy substituted with 0-2 R_6, and Y;

R_6 is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, $-S(O)_n(C_{1-4}alkyl)$, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, $CO(C_{1-4}alkyl)$, $CONH(C_{1-4}alkyl)$, $CON(C_{1-4}alkyl_1)(C_{1-4}alkyl_2)$ where $alkyl_1$ and $alkyl_2$ may be joined to form a heterocycle of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, $-XR_7$, and Y;

X is independently selected at each occurrence from the group consisting of $-CH_2-$, $-CHR_8-$, $-O-$, $-S(O)_n-$, $-NH-$, $-NR_8-$, $-C(=O)-$, $-C(=O)NH-$, $-C(=O)NR_8-$, $-S(O)_nNH-$, $-S(O)_nNR_8-$, $NHC(=O)-$, $-NR_8C(=O)-$, $-NHS(O)_n-$, and $-NR_8S(O)_n-$;

R_7 and R_8 are independently selected at each occurrence from hydrogen, and straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups, said straight, branched, and cyclic alkyl groups, and (cycloalkyl)alkyl groups

consisting of 1 to 8 carbon atoms, and containing zero or one or more double or triple bonds, each of which 1 to 8 carbon atoms may be further substituted with one or more substituent(s) independently selected from oxo, hydroxy, halogen, amino, cyano, nitro, haloalkyl, haloalkoxy, -O(C_{1-4}alkyl), NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl), -NHC(O)(C_{1-4}alkyl), -N(C_{1-4}alkyl)C(O)(C_{1-4}alkyl), -NHS(O)$_n$(C_{1-4}alkyl), -S(O)$_n$(C_{1-4}alkyl), -S(O)$_n$NH(C_{1-4}alkyl), -S(O)$_n$N(C_{1-4}alkyl$_3$)(C_{1-4}alkyl$_4$) where C_{1-4}alkyl$_3$ and C_{1-4}alkyl$_4$ are optionally joined to form a heterocycle consisting of from 5 to 8 ring atoms and containing 1, 2, or 3 heteroatoms independently selected from N, O, and S, and Y';

Y and Y' are independently selected at each occurrence from 3- to 8-membered carbocyclic or heterocyclic groups which are saturated, unsaturated, or aromatic, which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio;

wherein said 3- to 8-membered heterocyclic groups contain one or more heteroatom(s) independently selected from N, O, and S; and

n is independently chosen at each occurrence from 0, 1, and 2.

59. (Amended) A compound or salt according to Claim 58 wherein:

R_9 is selected from the group consisting of halogen, cyano, -$N(SO_2CH_3)_2$, -SO_2NH_2, halo(C_{1-3})alkyl, and C_{1-3}alkoxy.

62. (Amended) A compound or salt according to Claim 57, wherein:

R_9 is selected from the group consisting of halogen, cyano, -$N(SO_2CH_3)_2$, -SO_2NH_2, halo(C_{1-3})alkyl, and C_{1-3}alkoxy

R_{5B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, amino, C_{1-4}alkyl, and C_{1-2}alkoxy; and

R_{9B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, C_{1-2}alkyl, and C_{1-2}alkoxy.

63. (Amended) A compound or salt according to Claim 57, wherein:

R_5 is selected from the group consisting of bromo, fluoro, iodo, halo(C_{1-6})alkyl, halo(C_{3-6})alkoxy, C_{3-6}alkyl substituted with 0-3 R_6, C_{2-6}alkenyl substituted with 0-3 R_6, Y, -(C=O)Y,

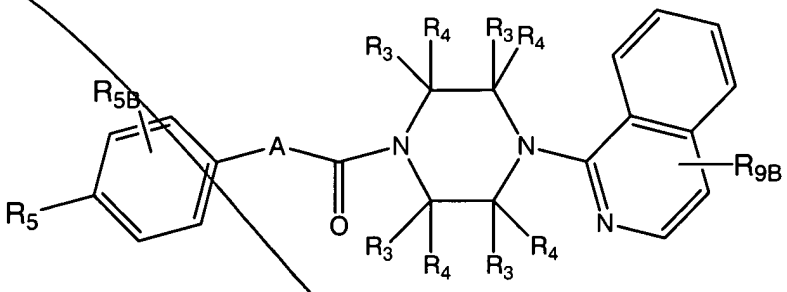
$-(CH_2)Y$, and $-(CH(CN))Y$;

R_9 is selected from the group consisting of halogen, cyano, $-N(SO_2CH_3)_2$, $-SO_2NH_2$, halo(C_{1-2})alkyl, and C_{1-3}alkoxy;

R_{5B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, amino, C_{1-4}alkyl, and C_{1-2}alkoxy; and

R_{9B} represents 0 or 1 substituents chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, C_{1-2}alkyl, and C_{1-2}alkoxy.

161. (Amended) A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, $CR_B\ R_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and C_{1-6} alkyl;

R_3 and R_4 are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl);

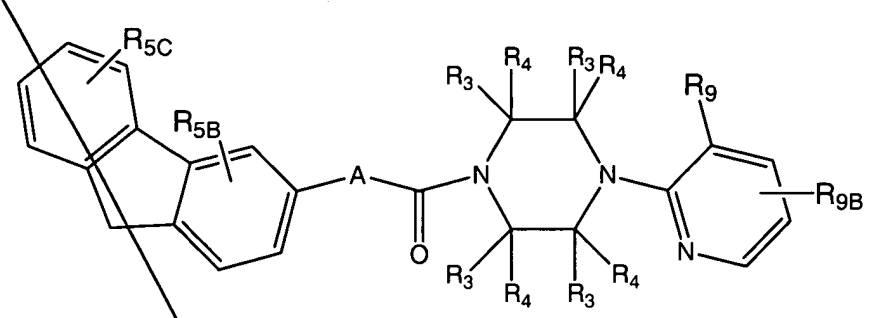
R_5 is selected from the group consisting of halogen, halo(C_{1-6})alkyl, C_{3-6}alkyl substituted with 0-3 R_6, C_{2-6}alkenyl substituted with 0-3 R_6, (C_{3-8}cycloalkyl)C_{1-4}alkyl substituted with 0-3 R_6, and Y;

R_{5B} and R_{9B} each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, amino, C_{1-4}alkyl, and C_{1-2}alkoxy;

R_6 is independently selected at each occurrence from the group consisting of cyano, halogen, hydroxy, C_{1-4}alkyl, C_{1-4}alkoxy, -NH(C_{1-4}alkyl), -N(C_{1-4}alkyl)(C_{1-4}alkyl) and Y;

Y is independently selected at each occurrence from C_{3-8} cycloalkyl, piperidinyl, piperazinyl, tetrahydropyranyl, dihydropyranyl, morpholinyl, thiomorpholinyl, phenyl, pyridyl, pyrazinyl, pyrimidinyl, thiazolyl, thienyl, and imidazolyl, each of which may be further substituted with one or more substituents independently selected from halogen, oxo, hydroxy, amino, nitro, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, halo(C_{1-4})alkyl, halo(C_{1-4})alkoxy, mono- or di(C_{1-4})alkylamino, and C_{1-4}alkylthio.

169. (Amended) A compound of the Formula:



or a pharmaceutically acceptable salt thereof, wherein:

A is absent or is selected from the group consisting of O, S, NR_A, CR_BR_B', $NR_ACR_BR_B'$, $CR_BR_B'NR_A$, $-CR_A=CR_B-$, and C_3H_4; where R_A, R_B, and R_B' are independently selected at each occurrence from hydrogen and C_{1-6} alkyl;

R_3 and R_4 are independently chosen at each occurrence from the group consisting of hydrogen, halogen, cyano, nitro, halo(C_{1-6})alkyl, halo(C_{1-6})alkoxy, hydroxy, amino, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{1-6}alkoxy, -NH(C_{1-6}alkyl), and -N(C_{1-6}alkyl)(C_{1-6}alkyl);

R_{5B}, R_{5C}, and R_{9B} each represent from 0 to 2 substituents and are independently chosen from halogen, cyano, nitro, halo(C_{1-2})alkyl, halo(C_{1-2})alkoxy, amino, C_{1-4}alkyl, and C_{1-2}alkoxy; and

R_9 is selected from the group consisting of halogen, cyano, -$N(SO_2CH_3)_2$, -SO_2NH_2, halo(C_{1-3})alkyl, C_{1-3}alkoxy, -NH(C_{1-3}alkyl), and -N(C_{1-3}alkyl)(C_{1-3}alkyl).

Please add new claims 199-209:

199. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or salt according to claim 4.

200. (New) A package comprising a pharmaceutical composition of claim 199 in a container and further comprising indicia comprising instructions for using the composition to alleviate pain.

201. (New) A package comprising a pharmaceutical composition of claim 199 in a container and further comprising indicia comprising instructions for using the composition to alleviate symptoms of exposure to capsaicin or tear gas.

202. (New) A compound or salt of claim 4 wherein, in an *in vitro* assay of capsaicin receptor antagonism, the compound or salt exhibits capsaicin receptor antagonist activity, but in an in vitro assay of capsaicin receptor agonism the compound does not exhibit detectable agonist activity.

203. (New) A compound or salt of claim 4 wherein a dose of the compound or salt that is twice the minimum dose sufficient to provide analgesia in an animal model for determining pain relief does not produce sedation in an animal model assay of sedation.

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204. (New) 4-(3-Chloro-2-pyridinyl)-N-[4-(isopropyl)phenyl]-1-piperazinecarboxamide or a pharmaceutically acceptable salt thereof.

Sub C1

205. (New) (2R)-N-(4-tert-butylphenyl)-4-[3-(dimethylamino)pyridin-2-yl]-2-methylpiperazine-1-carboxamide or a pharmaceutically acceptable salt thereof.

206. (New) (2R)-4-[3-(dimethylamino)pyridin-2-yl]-2-methyl-N-[4-(trifluoromethyl)phenyl]piperazine-1-carboxamide or a pharmaceutically acceptable salt thereof.

207. (New) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or salt according to claim 27.

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208. (New) A compound or salt of claim 27 wherein, in an *in vitro* assay of capsaicin receptor antagonism, the compound or salt exhibits capsaicin receptor antagonist activity, but in an in vitro assay of capsaicin receptor agonism the compound does not exhibit detectable agonist activity.

Sub C1

209. (New) A compound or salt of claim 27 wherein a dose of the compound or salt that is twice the minimum dose sufficient to provide analgesia in an animal model for determining pain relief does not produce sedation in an animal model assay of sedation.

B/7

210. (New) A package comprising a pharmaceutical composition of claim 207 in a container and further comprising indicia comprising instructions for using the composition to alleviate pain.

211. (New) A package comprising a pharmaceutical composition of claim 207 in a container and further comprising indicia comprising instructions for using the composition to alleviate symptoms of exposure to capsaicin or tear gas.

B